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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/100,812	06/19/98	GRAHAM M	11535

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SCULLY SCOTT MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY NY 11530

EXAMINER	
KAUSHAL,S	
ART UNIT	**PAPER NUMBER**
1633	7

DATE MAILED: 05/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/100,812	GRAHAM
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-33 is/are pending in the applicat

Of the above, claim(s) 6-33 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-5 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

The instant application claims priority to an Australian App. Ser. No. PP2292 filed 03/20/98.

Election/Restriction

2. Applicant's election with traverse of Group-I claims 1-5 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the claimed inventions are not independent and/or distinct. This is not found persuasive because inventions I-XXIX are independent and distinct. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the synthetic gene can also be delivered to cell via viral vectors, whereas plasmids can also be used as cloning vectors to make novel gene constructs. The plasmids of groups II-XXIX have different structure, function and are capable of exhibiting different effects in such a way that one is not required for other. Furthermore, these plasmid contain different genes sequences and cloning sites which are distinct in function and structure. For example, plasmid pEGFP-NI MCS contains CMV IE promoter operably connected to green fluorescent protein whereas pCMV.BEV.2 is capable of expressing BEV polymerase under the control of CMV IE promoter. Thus, inventions are distinct and are of separate use.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6, filed 04/12/00. Claims 1-5 are pending and are examined in this official action.

Claim Objections

1. Claim 5 is objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 5 have not been further treated on the merits.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 5 is rejected under 35 U.S.C. 101 because claim is drawn to **non-statutory subject matter**. The instant claim reads upon a cell, tissue organ or organism, which encompass humans. It is PTO policy not to allow claims to humans (1077 O.G. 24 April 1987). The insertion of "isolated" before cells, tissue or organ and "non-human" before organisms in the instant claim will overcome this rejection.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use the invention.**

The instant claims are drawn to a synthetic gene which is capable of modifying the target gene expression in a cell, tissue or organ of a prokaryotic or eukaryotic organism, wherein the synthetic gene sequence is substantially identical to the nucleic acid sequence of the target gene or a derivative thereof. The claims are drawn to the synthetic gene wherein the synthetic gene at least comprises multiple structural gene sequences. The claims are drawn to the synthetic gene wherein each of the structural gene is placed operably under the control of promoter sequence. The claims are drawn to a genetic construct comprising the synthetic gene of the invention and one or more origins of replication and/or selectable marker gene sequences. In addition the claims are drawn to a cell tissue, organ or organism comprising the synthetic gene(s) and genetic construct(s) describe herein.

The claimed invention, drawn to any and all synthetic genes or derivatives thereof is not enabled in view of the lack of teachings in the specification as filed regarding what additional sequences may be added to those specifically disclosed. The claim reads on number of non-enabled

embodiments such as a "gene" or "alleles". In view of fact that art does not provide an accepted definition for the term "gene", an elaboration of its characteristics (i.e. sequence) would require both a disclosure of a definition for the term and characterization of the synthetic gene sequence thereof. Furthermore, the invention as claimed read upon a combination of any and all multiple gene sequences, wherein the role of each component have not ascribed. It is known in the art that different genes have divergent functions. It is not clear how one skilled in the art would use the invention as claimed to modify what target genes in a cell, tissue, organ or organism.

6. The invention as claimed encompass on a method of delivering gene into an animal. The state of the art at the time of filing was such that **gene therapy** was regarded as highly unpredictable art because it has been difficult to predict the efficiency and out come of transduced therapeutic genes (Anderson WF, Nature 392:25-30, 1998; Verma et al Nature 389:239-242, 1997). The Recombinant DNA Advisory Committee (RAC) also emphasized that expectations of current gene therapy protocols have been over sold without any apparent success (Touchette, Nat. Med. 2(1) 7-8, 1996, page 7, col.1 para. 2; page 8, col.2 para 1-4). The advisory panel further emphasized the need for a greater understanding of an underlying mechanism that contribute to a genetic disease along with the pathogenesis of the disease. (Touchette, page 7, col.3, para.3). Furthermore, various factors govern the expression and/or therapeutic potential of transduced genes in vivo. Besides the lack of efficient delivery systems, lack of sustained expression and host immune reactions also remain formidable challenges (Verma et al, page 239 col.1 para.1). The instant specification fails to describe a single working example that demonstrated the sustained expression of any and all synthetic gene(s) in an animal wherein the synthetic gene is delivered to a target gene site via viral or non viral vector. In addition it is not clear how one skilled in the art would use the synthetic gene and/or combination thereof to modify the expression of what target gene of interest. The art clearly teaches that the delivery and expression of a therapeutic gene via gene therapy was not only problematic in past but is also the case in present despite the various advances in the field of gene therapy.

7. The instant invention as claimed encompass any and all **transgenic organisms** comprising the synthetic genes and genetic constructs. The state of transgenic art at the time of filing was such that transgene expression and physiological consequences of transgene products in non-mouse mammals are not always accurately predicted among various species of mammals (Wall RJ Theriogenology 45:57-68, 1996). Transgene efficiency is low and rage from 1% in farm animals (cattle, sheep, pigs) to 3% in laboratory animals like rabbits, mice and rats (Wall, see page 61). Furthermore, the lack of understanding of essential genetic control elements make it difficult to predict the behavior of a transgene in any and all animals because the expression is influenced by position effect in transgenic animals. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, are the important factors that govern the expression of a transgene (Wall, page 61-62). Furthermore, many biochemical pathways are plastic in nature which reflects the ability of the embryo to use alternative gene when the preferred gene is modified (Kappel et al. Current Opinion in Biotechnology 3:348-353 1992, page 550, col.1, para. 3-4). Furthermore, genetic modulation via homologous recombination is highly unpredictable art which requires numerous step that often fails because embryonic stem (ES) cells are very sensitive to culture conditions and have natural tendency to differentiate, giving rise to unstable genome. In addition, the homologous recombination is a rare event and the injection of ES in the blastocyte is highly unpredictable (Viville, in Transgenic Animals, Houdebine (eds), Harwood academic publishers, France. pp307-321, 1997).

8. Thus, in view of lack of specific guidance in the specification, the skilled artesian at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation. The quantity of experimentation required would include the functional and structural characterization of any and all synthetic gene(s) and their use in the modification of the target gene expression in any and all cell types, tissue types and organisms. The experimentation

would further include the development of methods to deliver identified synthetic gene to the target sites for the modification of the target gene expression. The quantitiy of experimentation required would also include making of any and all transgenic animals encoding any and all synthetic genes and/or synthetic gene constructs.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 5 is are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and **distinctly claim the subject matter** which applicant regards as the invention.

Claim 5 recites the limitation "described herein" in line 2. The instant claim is indefinite because it is unclear if it reference to the species or a claim. Furthermore, claims can only depends upon claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (PNAS 94:11563-11566, 1997). Wang et al teaches factor IX targeting vector with multiple structural gene sequences (page 11563 col.2 para.1; page 11564, fig-1). The cited art teaches a transgenic mice wherein the Factor IX gene has been disrupted by homologous recombination (page 11565, fig-2). Thus, the cited art anticipate the invention of instant claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-2035. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

S. Kaushal, AU 1633

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600